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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/286,189	08/05/94	SANHUEZA S	MISMS1038348

18M1/1126

SIM AND MCBURNEY
330 UNIVERSITY AVENUE
SUITE 701
TORONTO ON M5G 1R7
CANADA

EXAMINER	
MASOOD,K	
ART UNIT	**PAPER NUMBER**
1817	11

DATE MAILED: 11/26/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 10-3-96.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three month(s), ~~or thirty~~ days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-16 ~~is~~/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-16 ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Part III DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1817.

1. The amendment filed 10/3/96 has been received and entered. Claims 1-16 are pending in the application.

2. In view of applicants' amendments and arguments claims 1-16 rejected under 35 U.S.C. § 112, first paragraph has been withdrawn.

3. Claims 1-16 remain rejected under 35 U.S.C. § 103 for the reason presented at pages 7-15 of the Office Action 7/12/96.

Applicants arguments filed 10/3/96 have been considered but have not been found persuasive.

Response under 35 U.S.C. § 103 rejection:

Applicants traverse the rejection of claims 1 to 4, 15 and 16 over Bordt et al in view of Downing et al and further in view of McIntosh et al.

Applicants assert that the prior art does not suggest inactivation of the purified virus and there is a prejudice in the art for inactivation of the virus. Applicants further argue each reference individually.

Applicants arguments are not persuasive as stated in the previous Office Action. Downing et al teach purification of the virus free from cellular and serum components (see Office Action page 8, para 3, lines 3-6). Furthermore, Bordt et al teach inactivation of the virus with the ascorbic acid (see Office Action page 8, para3, lines 1-2). There was a expectation in the art regarding the use of inactivated virus before purifying the virus in a vaccine composition is discussed by Downing et al (see page 216, para 1, lines 9-11). Downing et al teach "one prerequisite for systematic biochemical and functional analysis of viruses is an abundant and very pure viral preparation, preferably one with infective virus particles; the efficient and effective purification schemes for enveloped viruses are important both clinically and for many research efforts especially for the development of strategies for disease intervention, particularly where traditional vaccines have not worked well; Respiratory syncytical virus (RSV)is an example of

an enveloped virus from the class of paramyoxoviridae; RSV causes respiratory infection that is both difficult to treat and is not currently amenable to prevention by vaccination" (see page 216, para 1, lines 1-18.

Formalin-inactivation caused disease potentiation partly due to the action on the F and G glycoproteins and impure viral preparation containing cellular or serum components (see page 3, para 3, lines 5-~~10~~ 30 of ~~last Office Action~~ Specification). Downing et al also addresses the issue why vaccines have not worked in the past partly due to impure viral preparation (see introduction section). One of ordinary skilled in the art would be motivated to purify the virus first to remove contaminants as suggested by Downing et al then inactivate the virus with the ascorbic acid or any other inactivating agent that has been used traditionally in the virology field. One of ordinary skill in the art would have expected that by purifying the virus first then inactivation of virus would be more efficacious since there is no contaminants.

McIntosh et al was incorporated to as evidence that one of ordinary skill in the art would have been motivated and expected to inactivate "human RSV" as set forth in the first Office Action (see page 9, first paragraph).

Applicant argues the references individually and not their combination. One cannot show non-obviousness by attacking

references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 159 USPQ 725 (CCPA 1968).

Accordingly, claims 1 to 4, 15 and 16 remain rejected under 35 U.S.C. § 103 over Downing et al in view of Bordt et al and further in view of McIntosh et al.

Applicants traverse the rejection of claims 5 and 6 based on the above arguments and assert that Preston et al and Downing et al do not provide expectation to use the β-propiolactone inactivation.

The teachings of Downing et al is set forth above and provide motivation (see also previous Office Action page 9, para 2, lines 1-6). The teachings of Preston et al have also been described in the previous Office Action (see page 9, para 3, lines 1-2). Preston et al was applied specifically for the use of β-propiolactone as an inactivating agent because Preston et al teaches that β-propiolactone is effective in inactivating RSV (see paragraph bridging p 819-820). One of ordinary skill in the art would inactivate a virus for an immunogenic composition to prevent the host from being infected with the virus despite it inhibits the T cell response and reduce resistance to RSV.

Applicants arguments are noted. The examiner acknowledges RSV response is inhibited by infectious RSV. However in a vaccine where the response is prior to infection the issue of infectious RSV inhibiting RSV-response of an inactivated RSV would not have been expected using β-propiolactone for vaccination. Therefore, applicants arguments regarding the different purpose of Preston study i.e. to inhibit the proliferative T-cell response to inactivated RSV is moot.

Accordingly, claims 5 and 6 remain rejected under 35 U.S.C. § 103 over Downing et al in view of Preston et al.

Applicants traverse the rejection of claims 5 and 9 based on the above arguments and assert that Downing et al do not teach inactivating the virus with ascorbic acid because of prejudice in the art against doing so and White et al reference is relied on for inactivation of the virus with ascorbic acid.

The teachings of Downing et al is set forth above and indeed, White et al was applied for inactivation of the virus with ascorbic acid (see previous Office Action page 10, lines 7-10). Applicants arguments are not commensurate with the claimed invention. The claimed invention is not drawn to inactivation as a vaccine. Further in view of inactivation with ascorbic acid is useful for serological assays wherein this antibody-antigen reaction it would have been reasonable for one ordinary skilled

in the art to expect to use ascorbic acid for vaccination wherein an antigen-antibody reaction takes place. Furthermore, applicants arguments of not yielding a preparation free of cellular contaminants are not persuasive because the claimed invention is not commensurate with the scope of the claims. The claimed invention only recites virus "substantially" free from cellular and serum components. Since it is not clear what constitutes "substantially", and clarification by centrifugation would result in a virus substantially free of contaminants as set forth by White et al the claimed invention is rendered obvious over the prior art.

Accordingly, claims 5 and 9 remain rejected under 35 U.S.C. § 103 over Downing et al in view of White et al.

Applicants traverse the rejection of claims 5, 7, and 8 over Downing et al in view of Prince et al and Georgiades et al. Applicants assertions are based on the same reasoning as stated above as for as Downing et al is concerned and further assert that Prince et al and Georgiades et al do not teach inactivation of the virus by non-ionic detergents, in particular glucopyranosides.

The teachings of Downing et al is set forth above. While it is true Prince et al teach inactivation of the hepatitis virus

with non-ionic detergents (see previous Office Action page 11, lines 1-6)since Downing et al suggest the use of non-ionic detergents including octyl glucoside for solubilization of viral preparation of VSV (see page 218, para 4, lines 1-5), it would have been expected non-ionic detergents would have inactivated the RS virus for the preparation of vaccine composition . Further while it is true that Prince et al teach inactivation of plasma hepatitis virus and Georgiades et al teach inactivation of contaminating viruses by non-ionic detergents respectively, one of ordinary skilled in the art would have been motivated and expected to use non-ionic detergents when the virus is first purified as suggested by Downing et al.

Accordingly, claims 5, 7 and 8 remain rejected under 35 U.S.C. § 103 over Downing et al in view of Prince et al and Georgiades et al.

Applicants traverse the rejection of claims 5, 10, 12 and 13 over Ewasyshyn et al in view of Mbiguino et al. Applicants assert that processing of the virus material by Ewasyshyn et al is different than from the claimed steps of the instant application and Mbiguino et al teaching is cumbersome and time-consuming.

As stated in the previous Office Action Ewasyshyn et al teach a method of preparing the virus as claimed in the instant

application (see page 11, para 3, lines 1-9)in conjunction with the teachings of Mbiguino et al (see page 12, lines 4-5).

Accordingly, claims 5, 10, 12 and 13 remain rejected under 35 U.S.C. § 103 over Ewasyshyn et al in view of Mbiguino et al.

The examiner notes applicants arguments that Ewasyshyn et al does not teach inactivation. However, Mbiguino et al teaches an inactivation by using non-ionic detergent conditions using a sucrose gradient. The examiner acknowledges Ewasyshyn et al does not teach of purifying the virus. However in view that Mbiguino et al teaches of a new method to obtain substantial amounts of purified RSV, one of ordinary skill in the art would have been motivated to use the method as set forth by Mbiguino et al. Applicants argue Mbiguino et al method is time consuming. However said arguments are not persuasive to overcome the rejection since: 1) there is no evidence the method is time consuming and; 2) it would reasonable to expect one of ordinary skill in the art would use said method as set forth by Mbiguino et al, since this method recovers RSV high titers of RSV (see abstract).

Applicants argue Mbiguino et al purification method is not vaccine development. Applicants arguments are noted. However applicants arguments are not persuasive since the claims are not drawn to a vaccine but an immunogenic composition. Since this method preserves viral infectivity (see page 169 and abstract)

would be expected the composition would be immunogenic as the claimed invention recites.

Applicants traverse the rejection of claim 11 over Ewasyshyn et al in view of Mbiguino et al and further in view of McIntosh et al and Paradiso et al. Applicants assert that Ewasyshyn et al and Mbiguino et al have deficiencies as discussed above by the applicants and therefore, McIntosh et al and Paradiso et al are not applicable.

Since the deficiencies of Ewasyshyn et al and Mbiguino et al by the applicants have been addressed above, the prima facie case of obviousness maintained.

Applicants traverse the rejection of claim 14 over Ewasyshyn et al in view of Downing et al and Kuchler. Applicants assert that deficiencies of Ewasyshyn et al and Downing et al have been discussed and Kuchler et al teaching is general method of purification steps and lack specific steps as claimed.

The teachings of Ewasyshyn et al and Downing et al are set forth above. Kuchler teachings have been described in the previous Office Action (see page 14, para 2, lines 1-6) which meet every limitation of the claim.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khalid Masood whose telephone number is (703) 305-6998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmission via the PTO Fax Center, located in Crystal Mall 1. The Fax Center number is (703) 308-4242. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

If attempts to reach the examiner by telephone are unsuccessful, the examiners's supervisor, Dr. Paula Hutzell, can be reached on (703)308-4310.

Khalid Masood, Ph.D.
November 1, 1996

ANTHONY C. CAPUTA
PRIMARY EXAMINER
GROUP 1800

RECEIVED
OCT 21 1997

Date: April 22, 1997 Our Ref: 1038-384 MIS:as
Applicant: Sonia E. Sanhueza et al
Application No: 08/286,189
Title: INACTIVATED RESPIRATORY SYNCYTIAL VIRAL VACCINES
New Appln, Cheque, Formal Papers: ( )
Date of Response: April 22, 1997
Retyping Required in Notice of Allowance: ( )
Final Fee: ( )
Other:
Due Date: April 26, 1997

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Please place the official stamp of the Patent Office on this card and return it to us for our files to constitute an acknowledgment by the Patent Office of receipt of the above-identified papers on the date stamped.

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